

**REMARKS/ARGUMENTS**

Claims 39-53, 57, 58 and 174-177 are pending in the application. Claims 57, 58 and 174-177 are allowed. Claims 39-53 are rejected. Claim 39 is amended herein. Support is provided at e.g., pp. 19-21. No amendment should be construed as acquiescence in any ground of rejection.

***Rejections under 35 USC §112***

The Examiner has rejected claims 39-53 as being indefinite because of a lack of clear connection between the computer system limitation and the probes on the array. The claim has been amended to clarify the connection between the computer system limitation and the probes on the array. Applicants have amended claim 39 to clarify that the array is designed by using a computer system to query a sequence database to identify the sequence and size of fragments that will result when the nucleic acid sample is digested with the selected restriction enzyme. The computer system is then used to identify fragments in a selected size range and then to identify known polymorphisms on those fragments. The array is then designed to interrogate the genotypes of identified polymorphisms.

The computer system is used to identify a collection of polymorphisms that are predicted to be present on amplified fragments given the selected fragmentation and amplification method and the probes of the array are selected to interrogate a subset of the polymorphisms in that collection. The nucleic acid sample is treated using the same selected fragmentation and amplification method so the fragments containing the polymorphisms interrogated by the array should be amplified in the second sample.

The computer system identifies the polymorphisms that are predicted to be present in the amplified fragments based on the size of restriction fragments that will be amplified and identification of polymorphic markers that are present in those fragments in a human population, using a database of known polymorphisms. The array has probes to interrogate the genotypes of at least a subset of the first set of polymorphisms to determine which allelic form or forms are

present in the sample. Probes to interrogate the genotype of polymorphisms that are on fragments that are NOT predicted to be amplified, because the fragments are too long or too short, are NOT included on the array.

For the above reasons, withdrawal of the rejection of claims 39-53 is respectfully requested.

***Rejections under 35 USC §102***

Claims 39-45, and 48-53 have been rejected over Sapolsky et al. (U.S. Patent No. 5,710,000).

Claim 39, from which claims 40-45 and 48-53 depend has been amended to specify a process by which probes are selected in an array used to analyze fragments resulting from complexity reduction. In brief, a sequence database is queried to identify the size and sequence of fragments that are predicted to result from digestion of an initial substrate. The computer then selects a subset of these fragments within a given size range (these being within the size range predicted to survive the selective amplification process). The computer identifies known polymorphism in the these fragments. Probes are then selected to be complementary to the identified polymorphisms.

Sapolsky discloses a different approach for designing an array. Sapolsky discusses providing a set of  $4^k$  probes for sequences of length  $k$  (see col. 12, lines 15-60). Such a probe set contains all probes of a given length. Because all probes of a given length are present, such an approach does not require any assumptions or predictions of which fragments survive complexity reduction. Accordingly, this approach does not disclose or suggest the selection of probes as recited in the amended claims.

***Rejections under 35 USC §103***

Claims 46 and 47 have been rejected over Sapolsky et al. (U.S. Patent No. 5,710,000) in view of Kato (EP 0 735 144 A1). Kato is cited as teaching that the method can be conducted on cDNA derived from mRNA. However, Kato does not compensate for the deficiency in Sapolsky with respect to the amended claims, as noted above.

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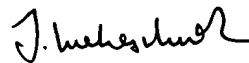
***Double Patenting***

Claims 39-53 are provisionally rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claim 39 of co-pending Application No. 10/316,881, Title: "Information processing system, method and recording medium for controlling same". Applicants believe that the Examiner may have intended to base the provisional rejection on claim 39 of co-pending application No. 10/316,811, Title: "Complexity management of genomic DNA by semi-specific amplification." Applicants request clarification.

Once allowable subject matter has been indicated, Applicants will consider submitting a terminal disclaimer, as may be appropriate. Applicants request that this rejection be held in abeyance until allowable subject matter is indicated.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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